Interventional procedure overview of percutaneous thrombectomy for massive pulmonary embolism

Contents

Table 1 Abbreviations

Abbreviation	Definition
CDT	Catheter-directed thrombolysis
CTPA	CT pulmonary angiogram
DVT	Deep vein thrombosis
ECMO	Extracorporeal membrane oxygenation
ICU	Intensive care unit
LBAT	Large bore aspiration thrombectomy
LV	Left ventricular
MAE	Major adverse event
mPAP	Mean pulmonary artery pressure
MT	Mechanical thrombectomy
PE	Pulmonary embolus
RC	Routine care
RV	Right ventricular
RV/LV ratio	Right ventricular (RV)/ Left ventricular (LV) ratio
SAE	Significant adverse event

Indications and current treatment

A pulmonary embolism (PE) is an obstruction of a pulmonary artery usually caused by an embolus that travels to the lungs from deep veins in the leg or pelvis. Pulmonary embolism often causes shortness of breath, chest pain and cough. The symptoms and severity vary from no symptoms to cardiovascular collapse and death. A massive PE is defined by sustained systemic hypotension or shock (high-risk PE). A sub-massive PE involves right ventricular dysfunction or myocardial injury but without haemodynamic compromise (intermediate-risk PE).

Massive PE accounts for less than 10% of acute PE cases and is a medical emergency with a high mortality rate. The first-line treatment for PE is systemic anticoagulants. In cases of massive or sub-massive PE, systemic thrombolysis may be used, and rarely

open surgical embolectomy is performed. Catheter-directed therapies may be used which include catheter-directed thrombolysis (CDT) and percutaneous thrombectomy. Percutaneous thrombectomy is usually used for patients who have suffered a massive PE and in whom thrombolysis is contraindicated or has failed and who are not candidates for surgery.

What the procedure involves

In this endovascular procedure, a catheter is inserted percutaneously into the peripheral vasculature (usually via a common femoral vein) and advanced through the right side of the heart into the pulmonary arteries under image guidance. This procedure is usually performed by interventional radiologists and interventional cardiologists. It is usually done using local anaesthesia with or without sedation.

There are several thrombectomy devices available with some variation in their mechanism. The thrombus may either be fragmented before removal or not. There are several methods by which the thrombus can be removed: vacuum suction, aspiration with a syringe, mechanical removal with a clot removal device or a combination of methods. It is a minimally invasive procedure which may be used alone or in combination with other treatment options for PE.

The aim of the procedure is to rapidly remove the obstruction and restore pulmonary circulation, reducing right ventricular strain, whilst avoiding the bleeding risks associated with thrombolysis.

Outcome measures

The main outcome measures included right ventricular (RV)/left ventricular (LV) ratio, pulmonary artery pressure, modified Miller score, cardiac index, RV systolic pressure, and CT obstruction index. The measures used are detailed in the following paragraphs.

RV/LV ratio

RV/LV ratio can be measured by CT, echocardiography or as a composite measure. A meta-analysis found that, across all CT parameters reviewed as potential predictors of outcome in acute PE, RV/LV diameter ratio had the strongest predictive value for adverse clinical outcomes and mortality (Meinel 2015). It has also been used in multiple studies of various PE treatments as a marker of treatment effectiveness. For comparison, a meta-analysis of CDT reported a mean reduction of RV/LV ratio of 0.34 (Bloomer 2017).

Pulmonary artery pressure

Usually reported as mean pulmonary artery pressure (mPAP), this outcome measure is used by multiple studies of the effectiveness of treatment in acute PE. Echocardiography is generally used to measure systolic pulmonary artery pressure and raised mPAP is a key feature of acute PE. Pre- and post-procedure mPAP is commonly reported, and some studies include later follow-up of this outcome measure.

Modified Miller score

The modified Miller score is a measure of thrombus burden according to CT pulmonary angiogram (CTPA) imaging which is used in acute PE. The extent of thrombus in each part of the pulmonary arteries is scored from 0 (none) to total occlusion (3), out of a maximum of 16. There is also a refined modified Miller score which has a maximum score of 40.

CT obstruction index

The CT obstruction index is another scoring system for thrombus burden on CT imaging (Qanadli 2001). The system assigns a heavier weighting to full vessel occlusion than to partial occlusion. However, there have been conflicting results

on the ability of this scoring system to predict mortality in acute PE (Vedovati 2013).

Cardiac index

The cardiac index is a haemodynamic parameter that is a measure of cardiac function. Specifically it is a measure of cardiac output that normalises the cardiac output value according to body size. The normal range for this measure is 2.6 to4.2 L/min/m^2. The equation for calculating this measure is:

Cardiac index = cardiac output/body surface area = (stroke volume x heart rate)/body surface area

Major adverse event (MAE) rate

The MAE rate is a composite measure used in studies to detail the rate of MAE, the components of which vary by study.

Evidence summary

Population and studies description

This interventional procedures overview is based on 531 patients and 67 'events' from 2 single-arm trials (1 trial included with its sub-study), 1 safety database review, 1 retrospective comparative study and 1 prospective registry. Of these 531 patients, 501 patients had the procedure and 67 events in the MAUDE database referred to this procedure. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 6 studies as the key evidence in table 2 and table 3, and lists 29 other relevant studies in table 5.

Of the 6 included studies, all were from the USA. Of the 6 studies, all reported follow-up outcomes of various durations except the MAUDE database review. Four reported 30-day follow-up periods and 1 reported 6-month follow-up.

All studies reported inclusion criteria, but these varied, as did terminology for the level of risk of PE in participants. Excluding the MAUDE database review which

did not specify, 3 studies referred to intermediate or submassive PEs only and 2 included both intermediate and high-risk PEs. Across the 5 studies reporting age of participants, the average age ranged from 55.6 to 73.8 with a slight majority of male patients. Table 2 presents study details.

Figure 1 Flow chart of study selection

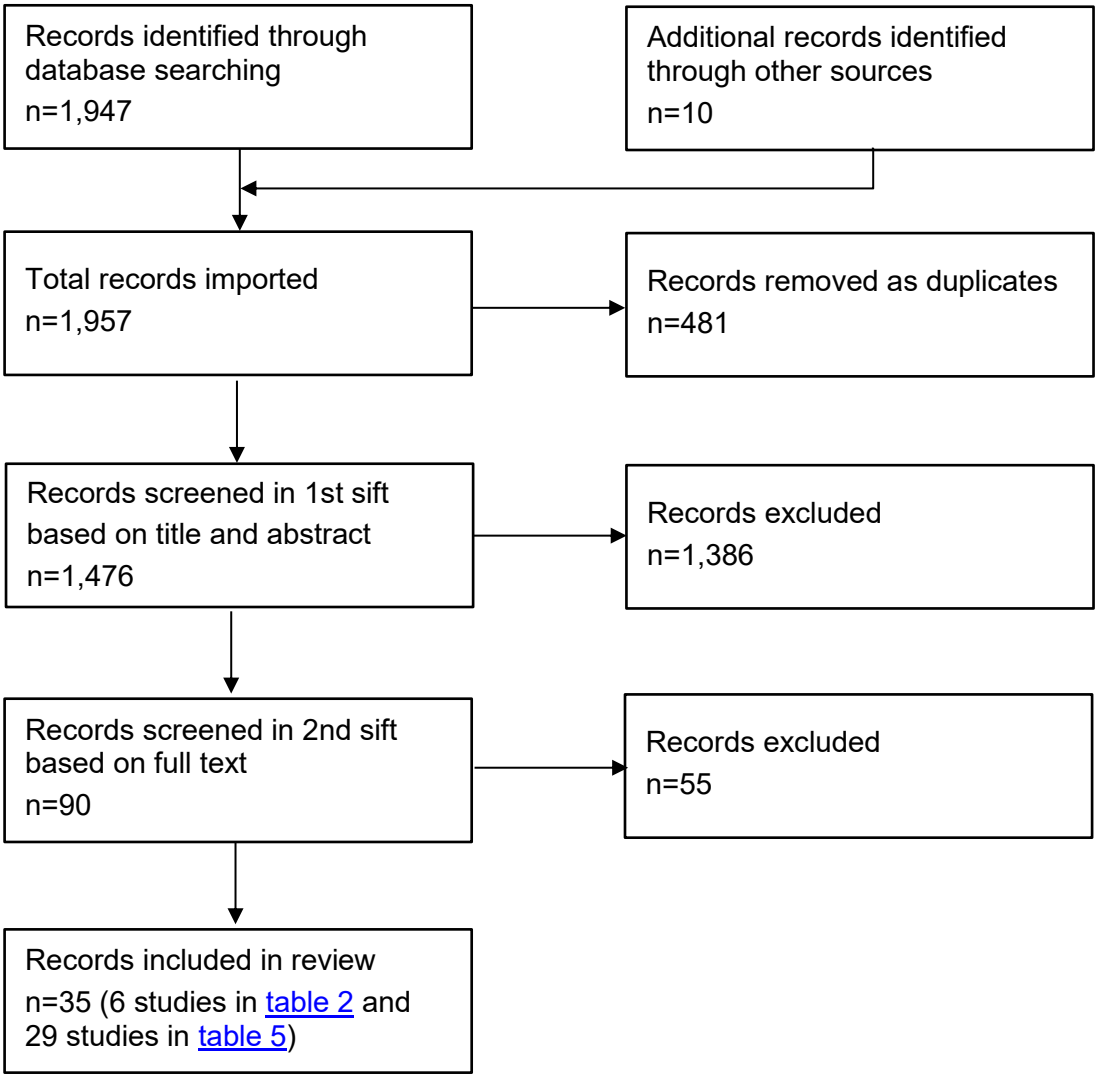

Table 2 Study details

IP overview: percutaneous thrombectomy for massive pulmonary embolism

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
1	Toma, 2022 USA	N=250 (131:119)	Mean 60.9	Prospective multicentre registry in real-world population (single-arm)	Age >18, clinical signs and symptoms of acute PE with evidence proximal filling defect in at least 1 main/lobar PA and who were undergoing treatment with FlowTriever. 6.8% high-risk and 93.2% intermediate-risk	FlowTriever System (Inari Medical)- percutaneous mechanical thrombectomy	48 hours, 30 days and 6 months

2	Sista, 2021 USA	N=119 66:53	Mean 59.8	Prospective, single-arm, multicentre investigational device exemption trial	Submassive PE 1. Clinical signs and symptoms consistent with acute PE with duration of 14 days or less. Evidence of PE must be from CTPA 2. Systolic BP ≥90 mmHg with evidence of dilated RV with an RV/LV ratio >0.9 3. 18 years of age or older	Penumbra Indigo aspiration system-suction embolectomy device	Intraprocedural, at 48 h, at discharge, and at 30 days
3	Tu, 2019 USA	N=104 (56:48)	Mean 55.6	Prospective single-arm multicentre investigational device exemption trial	Intermediate-risk patients. Ages 18 to 75, PE symptoms ≤14 days, symptomatic, CT-documented proximal PE, haemodynamically stable (no vasopressor requirement, heart rate <130, systolic blood pressure	FlowTriever System (Inari Medical)-percutaneous mechanical thrombectomy	48 hours and 30 days

					≥90 mmHg at baseline assessment) and RV/LV ratios ≥0.9 (on basis of CT). Acute intermediate-risk PE.		
4	Buckley, 2022 USA	N=58: Mechanical thrombectomy (MT) N=28 (46% Female) Routine care (RC) N=30 (67% Female)	MT 68.8±14.3 RC 73.8±12.7	Retrospective single-centre comparative study	Pulmonary Embolism Severity Index (PESI) score of 4 or 5 and European Society of Cardiology (ESC) classification of intermediate-high or high risk; acute, central PE (defined as thrombus within the pulmonary trunk, left/right main pulmonary artery, truncus anterior, or interlobar pulmonary artery); RV:LV ratio >1; and who were treated as inpatients.	FlowTriever System (Inari Medical)-percutaneous mechanical thrombectomy	To 30 days

					Additionally technical success (successful delivery of the device to the pulmonary arteries with extraction of clot) for the MT group. 80% of RC group treated with anticoagulation alone, 13% with systemic thrombolysis and 7% with anticoagulation and CDT.		
5	Jaber, 2020 USA (sub-study of Tu, 2019)	N=76 44:32	Median age 56	Multi-centre single arm prospective trial: sub-study	Acute intermediate-risk PE. Emergency department (ED) patients with acute PE (that is diagnosed with PE in ED) and RV/LV ratio ≥0.9 enrolled in the FLARE study (Inclusion criteria for this study seen listed in Tu, 2019).	FlowTriever System (Inari Medical)- percutaneous mechanical thrombectomy	48h, 30 days

6	Sedhom, 2021 USA	N=67 events (over 20 months)	Not documented	Manufacturer and User Facility Device Experience (MAUDE) FDA database review (real world data)	Reports related to the use of the device in the pulmonary vasculature. MAUDE database reporting is either mandatory (for manufacturers and device user facilities) or voluntary (for healthcare professionals, patients, and consumers)	Penumbra Indigo aspiration system-suction embolectomy device	No follow-up

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Toma, 2022	**Secondary endpoints: intra-procedural changes in haemodynamics, markers of cardiac size and function at follow up as measured by**	**Primary endpoint**: **Major adverse event rate (MAE)- composite of MAE within 48 h of the index procedure consisting of device-related**

	echocardiography, thrombectomy time, estimated blood, length of stay, and dyspnoea: **mPAP:** statistically significant intra-procedural reduction of 7.1 mmHg (22.2%, p<0.001). **Cardiac index:** overall no statistically significant change (n=202) pre- and post-procedure, but there was a statistically significant change in the low baseline cardiac index group: statistically significantly improved by 13.3% on-table from 1.7±0.2 to 1.9±0.4 l/min/m2 (p=0.005). **Heart rate:** decreased statistically significantly during hospitalisation by 13.5 bpm (12.6%, p<0.0001). **Dyspnoea:** decreased statistically significantly in those dyspnoeic before thrombectomy from 2.9±1.1 preprocedure to 1.4±1.3 at 48 h (p<0.001). **Mean length of stay:** 3 days post-procedure. 56.8% did not require ICU post-procedure. **Mean RV/LV ratio:** statistically significantly decreased by 0.36±0.76 (28.3%) from 1.27±0.26 pre-procedure to 0.91±0.75 at follow-up (p<0.001) (n=86). **RV systolic pressure:** statistically significantly decreased by 19.1±15.6 mmHg (35.8%) from 53.3±14.2 mmHg pre-procedure to 33.5 ± 11.9 mmHg at follow-up (p<0.001).	**death, major bleeding, and device- or procedure-related adverse events:** 3 MAEs (1.2%): all major bleeds that resolved without sequalae following transfusion. **Intraprocedural device- or procedure-related adverse events:** No device-related injuries, clinical deteriorations or deaths at 48 h. Median estimated blood loss 255.0 ml (100 to 425ml). **Secondary endpoints: individual components of the MAE composite, major access-site complications, all-cause mortality through 30 days, and device-related serious adverse events (SAE) within 30 days:** All-cause mortality was 0.4% at 30 days (single death unrelated to PE). One access-site complication (0.4%): haematoma in patient who received thrombolytics as well. 12 other non-device-related SAEs at 30 days. 30-day readmission rate: 13/216 (6.0%), only one of which (0.5%) related to PE.
Sista, 2021	**Primary endpoint: change in RV/LV ratio from baseline to 48 h post-procedure (computed tomography angiography)**	**Primary endpoint: composite of 48-h MAEs: device-related death, major bleeding, and**

IP overview: percutaneous thrombectomy for massive pulmonary embolism

	Mean RV/LV ratio reduction 0.43 (95% CI 0.38 to0.47; p<0.0001), representing 27.3% reduction (95% CI 24.83 to 29.67%). **Secondary endpoints:** Intraprocedural thrombolytics used in 2 patients (1.7%) 73 required ICU stay (61%) and median stay was 1.0 day mPAP reduction post-aspiration: 4.3 mmHg (95% CI: 2.6 to 5.9 mm Hg; 7.9% reduction; p<0.0001) mPAP reduction post-procedure: 4.7 mmHg (95% CI: 3.0 to 6.4 mmHg; 8.7% reduction; p<0.0001) Mean reduction in CT obstruction index from pre-procedure to 48-h follow-up was 11.3% (p<0.0001).	**device-related serious adverse events (clinical deterioration, pulmonary vascular, or cardiac injury)** 2 (1.7%, 95% CI 0.0 to 4.0%) patients experienced 3 MAEs: 1 patient experienced haemoptysis and access-site bleed, post-procedure death (ventricular tachycardia likely related to RV ischaemia from RV overload and haemorrhage). 1 patient experienced access-site bleeding only. **Primary endpoint:** Device-related SAEs within 48 h = 0.8% (95% CI 0.0 to 2.5%), a composite of: device-related clinical deterioration within 48 h 0.8% (1/119), device-related pulmonary vascular injury within 48 h 0.8% (1/119), device-related cardiac injury within 48 h 0%. **Secondary safety endpoints:** **At 48 h rates of:** cardiac injury 0%, pulmonary vascular injury 1.7%, clinical deterioration 0.8%, major bleeding 1.7%, and device-related death 0.8%. **At 30 days rates of:** Any cause-mortality 2.5% (95% CI 0.0 to 5.3%), device-related SAEs 1.7%, symptomatic recurrence of PE 0%.

		73.1% of patients had an estimated overall blood loss <400ml, 26.9% had >400ml but none required transfusion. 3 (2.5%) patients required transfusion related to the procedure.
Tu, 2019	**Primary effectiveness endpoint: change in RV/LV ratio from baseline to 48h** (±8 h or discharge): RV/LV ratio 1.56 at baseline, 1.15 at 48 h, average reduction of 0.38 (p<0.0001) that is 25.1%. **Mean pulmonary artery pressure (mPAP):** 29.8 mmHg pre-procedure vs 27.8 post-procedure (p=0.001). Effect driven by patients with pulmonary hypertension on presentation (n=70): 3.2 mmHg reduction (p<0.0001). **Refined modified Miller score (thrombus burden):** Pre-procedural score 20.8±2.4 vs 18.9±2.9 at post-procedure; p<0.001. **Length of ICU stay** 1.5±2.1 days Forty-three patients (41.3%) did not require any intensive care unit stay. **Length of hospital stay** 4.1±3.5 days	**Primary safety endpoint: composite MAE rate (any of following within 48 h: device-related death, major bleeding,** **treatment-related clinical deterioration, treatment-related pulmonary vascular injury, and treatment-related cardiac injury):** Composite MAE rate within 48 h 3.8% (n=4 patients experiencing 6 MAEs): • Clinical deterioration n=4 • Major bleeding event n=1 • Pulmonary vascular injury n=1 Major bleeding rate 0.9%. **Secondary safety endpoint: All primary safety events as well as mortality, device-related SAEs and symptomatic recurrence of embolism within 30 days:** An additional 10 patients experienced SAEs within 30 days. Total = 14 patients experienced 26 SAEs within 30 d, 5 experienced multiple SAEs.

		1 death at 23 d (respiratory failure from undiagnosed cancer).
Buckley, 2022	**Secondary endpoints: ICU length of stay, total hospital length of stay:** Average ICU length of stay statistically significantly lower for mechanical thrombectomy (MT) group vs routine care (RC) (2.1 ±1.2 vs 6.1±8.6 days, p<0.05). No statistically significant difference in total hospital length of stay (7.7±6.9 days in MT, 6.8±6.9 in RC).	**Primary endpoint: in-hospital mortality:** In-hospital mortality was statistically significantly lower for MT group vs routine care RC (3.6% vs 23.3%, p<0.05). **Secondary endpoints: 30-day readmission rate:** No statistically significant difference (11% in MT, 13% in RC). RC group: 3 self-limited bleeding complications not requiring transfusion (10%) and 1 case of haemodynamically significant bleeding requiring transfusion and endoscopy (3.3%). MT group: 3 procedure-related complications (10.7%; 1 self-limited haemoptysis, 2 post-procedure transfusions due to aspiration-related blood loss).
Jaber, 2020	**Primary endpoint: change in the RV/LV ratio from baseline to 48 h post-procedure** Reduction in median RV/LV ratio of 0.37 from 1.50 pre-procedure (range 0.88 to 2.52) to 1.13 post-procedure (range, 0.66 to 1.81), (p<0.001). **Secondary endpoints:**	**Primary endpoint: composite MAEs including major bleeding, device-related death or clinical deterioration, and vascular or cardiac injury within 48 h.** 3 MAEs (4%): 2 periprocedural respiratory deterioration requiring intubation, 1 major bleeding (leading to lobectomy), 1 patient

	Change in RV/LV ratio of patients with non-elevated cardiac troponin and zero simplified PE Severity Index (sPESI) score i.e. normal cTn-sPESI: intermediate-low risk (n=17, 22.4%) Reduction in mean RV/LV ration of 0.27 (p<0.001) **ICU stay:** 53% admitted to ICU post-procedure, median length of stay 1 day (range 0 to 11 days). **Heart rate:** median 91 bpm (55 to 123) to 89 (62 to 118) at 48 h. **Median PAP:** 30 mmHg (range, 7 to 57 mmHg) at presentation and 27 mmHg (range, 9 to 50 mmHg) after the procedure (p=0.533, NS). In 52 patients with elevated PAP (68.4%): statistically significant reduction in median PAP (34 to 31 mmHg, p=0.003).	experienced pulmonary vascular injury. All adjudicated as procedure-related rather than device-related. **Secondary endpoints:** **All-cause mortality** 100% survival to 30 days **Symptomatic recurrence PE within 30 d** None
Sedhom, 2021	**None reported**	**Primary outcome: mechanisms of failure of Penumbra Indigo aspiration system** Most common failure mode: Lightning Unit malfunction (35.8%, n=24) (tubing with dual pressure sensors with a built-in microprocessor for real-time blood flow monitoring). Rotating haemostasis valve malfunction (31.3%, n=21) Resistance during use (15%, n=10) Aspiration failure (11.9%, n=8) Engine malfunction (9%, n=6)

		Catheter clogging with thrombi (7.5%, n=5) Catheter kinking (6%, n=4) Engine canister malfunction (4.5%, n=3) Catheter broken (4.5%, n=3). **Secondary outcome: clinical consequences of device failure** Death (4.5%, n=3); 2 from fatal pulmonary vessel perforation (3%) and 1 from fatal right-sided heart failure (1.5%). Pericardial effusion (1.5%, n=1) Procedure aborted (6%, n=4) No need for ECMO, no haemoptysis, no intracranial bleeding and no blood transfusions.

Procedure technique

Of the 6 studies, all detailed the devices used and 5 detailed the procedure technique. Four studies used the Inari FlowTriever device for mechanical thrombectomy (Tu 2019, Toma 2022, Buckley 2022, Jaber 2020). Two studies used the Penumbra Indigo aspiration system for aspiration thrombectomy (Sedhom 2021, Sista 2021).

Aspiration thrombectomy involves the aspiration of thrombi through an aspiration catheter. Mechanical thrombectomy involves mechanical engagement of the thrombus and removal. Rheolytic thrombectomy includes the use of high-pressure jets of saline to disperse the thrombus followed by aspiration. The jets can consist of saline, but local thrombolytic agents can also be used. There are multiple different devices with other mechanisms associated with this procedure, some of which are no longer in use.

Efficacy

RV/LV ratio

This outcome was reported in 4 studies. All 4 found a statistically significant reduction in RV/LV ratio from baseline to follow-up. With the FlowTriever, Tu (2019) found a mean reduction of 0.38 ($p<0.0001$) at 48 hours and Toma (2022) found an average reduction of 0.36 ($p<0.001$) at follow-up (variable follow-up times, median 32 to 33.5 days). In the Jaber (2020) sub-study of FLARE population, reduction was 0.37 at 48 hours ($p<0.001$). Jaber (2020) also reported the change in RV/LV ratio for the intermediate-low risk sub-group of the study ($n=17$) and found a smaller but still statistically significant reduction of 0.27 ($p<0.001$). Sista (2021) reported a reduction of 0.43 ($p<0.0001$) at 48 hours with the Indigo system.

Pulmonary artery pressure

This outcome was reported in 4 studies. Tu (2019) reported a statistically significant reduction in mPAP (29.8 to 27.8 mmHg), p=0.001. The effect was driven by patients with raised mPAP on presentation in which subgroup there was a 3.2 mmHg reduction (p<0.0001). Toma (2022) reported a statistically significant intraprocedural reduction of 7.1 mmHg (p<0.001). In the Jaber (2020) sub-study, the median PAP demonstrated a statistically non-significant reduction of 3 mmHg (from 30 to 27 mmHg, p=0.533), although in the 52 patients with elevated PAP on presentation, there was a statistically significant reduction of 3 mmHg (34 to 31 mmHg, p=0.003). Sista (2021) reported a reduction in mPAP of 4.3 mmHg post-aspiration (p<0.0001) and of 4.7 mmHg post-procedure (p<0.0001), both statistically significant.

Length of stay

This outcome was reported in 5 studies. Tu (2019) reported an average length of ICU stay of 1.5±2.1 days, and hospital stay of 4.1±3.5 days. Toma (2022) reported a mean length of hospital stay of 3 days post-procedure and in the Jaber 2020 sub-study, a median length of ICU stay of 1 day is reported. In Sista (2021), 61% required ICU care and the median stay was 1.0 day.

Buckley (2022) reported an average length of ICU stay of 2.1±1.2 days which is statistically significantly lower than the ICU length of stay for the routine care group (vs 6.1± 8.6 days, p<0.05). There was, however, no statistically significant difference in hospital stay between the 2 groups, with the mechanical thrombectomy group staying in hospital on average 7.7±6.9 days overall. These hospital length of stay figures are higher than reported by the other studies.

Modified Miller score

This outcome was reported in 1 study. Tu (2019) use the refined modified Miller score and reported a pre-procedural score of 20.8±2.4 vs a post-procedural score of 18.9±2.9, representing an average reduction of 1.9 ($p<0.001$).

CT obstruction index

This outcome was reported in 1 study. Sista (2021) reported a mean reduction in CT obstruction index of 11% at 48 hours ($p<0.0001$).

Cardiac index

This outcome was reported in 1 study. Toma (2022) reported overall no statistically significant change in cardiac index between pre- and post-procedure. However, there was a statistically significant improvement in cardiac index in the sub-group with low baseline cardiac index (that is, impaired cardiac function). In this group cardiac index improved by 13% on-table ($p=0.005$).

Safety

Major adverse event rate

Four studies reported a composite MAE rate as their primary safety endpoint. The composition of this MAE rate varied by study but was similar, usually including major bleeding, device-related death or clinical deterioration and injury to vessels/the heart/the lungs. The composite measure is discussed followed by the individual measures.

Tu (2019) reported a composite MAE rate (device-related death, major bleeding, treatment-related clinical deterioration, treatment-related pulmonary vascular injury, and treatment-related cardiac injury) of 4% (n=4) at 48 hours. Toma (2022) reported an MAE rate (device-related death, major bleeding, and device-

or procedure-related adverse events) of 1% (n=3) at 48 hours, all major bleeding events but with no device-related injuries, clinical deteriorations or deaths at 48 hours. Jaber (2020), in their sub-study of the FLARE population (Tu 2019), reported an MAE rate (major bleeding, device-related death or clinical deterioration, and vascular or cardiac injury) of 4% (n=3) at 48 hours. Sista (2021) reported an MAE rate (device-related death, major bleeding, and device-related serious adverse events [clinical deterioration, pulmonary vascular, or cardiac injury]) of 3 MAEs in 2 patients (2%) at 48 hours.

Major bleeding

Six studies reported on bleeding-related complications. Tu (2019) reported 1 major bleeding event in 104 patients at 48 hours. Toma (2022) reported a 1% major bleeding rate (n=3). Buckley (2022) did not classify bleeding complications by severity but reported 3 procedure-related complications in the mechanical thrombectomy group (11%): 1 self-limited haemoptysis and 2 post-procedure transfusions due to aspiration-related blood loss. In the routine care group the rate was similar with 3 self-limited bleeding complications not requiring transfusion (10%) and 1 significant bleed requiring transfusion (3%). Jaber (2020) reported 1 major bleeding event which was procedure-related at 48 hours in a study of 76 patients. Sista (2021) reported 2 instances of major bleeding (2%) and 3 patients requiring transfusion related to the procedure (3%). Sedhom (2021)reported no haemoptysis episodes, no intracranial bleeding and no episodes requiring blood transfusion.

Clinical deterioration

Four studies specifically reported a clinical deterioration rate**.** Tu (2019) reported a clinical deterioration rate of 4% (n=4) at 48 hours and in the sub-study, Jaber (2020), reported 4% (n=3) at 48 hours. Toma (2022) reported a clinical

deterioration rate of 0% at 48 hours. Sista (2021) reported 1 episode of clinical deterioration at 48 hours in 119 patients.

Pulmonary vascular injury

Five studies reported on instances of pulmonary vascular injury**.** Tu (2019) reported 1 pulmonary vascular injury in 104 patients at 48 hours and Jaber (2020) also reported 1 pulmonary vascular injury in their sub-study of 76 patients, which likely represents the same patient. Sedhom (2021) reported 2 pulmonary vessel perforations (3%). Sista (2021) reported 2 instances of pulmonary vascular injury (2%) at 48 hours, 1 of which (1%) was device-related. Toma (2022) reported 0 device-related pulmonary vascular injuries.

Cardiac injury

Five studies reported on cardiac injury. Tu (2019), Jaber (2020), Toma (2022), Sista (2021) and Sedhom (2021) all reported no episodes of cardiac injury.

Mortality

All 6 studies reported measures of mortality. Tu (2019) reported 1 death during follow-up (1%) at 23 days post-procedure, attributed to respiratory failure from undiagnosed cancer and so unrelated to the procedure. Toma (2022) reported 1 death in a study of 250 participants at 30 days which was unrelated to the procedure. Buckley (2022) reported in-hospital mortality of 4% for the mechanical thrombectomy group, which was statistically significantly lower than the routine care group (23%, $p<0.05$). Sedhom (2021) reported 3 deaths (5%): 2 from pulmonary vessel perforation (3%) and 1 from right-sided heart failure (2%). Jaber (2020) reported 100% survival at 30 days. Sista (2021) reported 1 post-procedure device-related death (1%) related to haemorrhage and right ventricular overload at 48 hours and a 3% rate of any cause mortality at 30 days (n=3).

Access-site complications

Access-site complications may include bleeding, nerve injury and damage to other structures, for example arteries. Two studies reported access-site complications. Toma (2022) reported 1 access-site haematoma in a patient who also received thrombolytics in 250 participants. Sista (2021) reported 2 patients (2%) experiencing access-site bleeding.

30-day readmission rate

Two studies discussed 30-day readmission rates. Toma (2022) reported a 30-day readmission rate of 6% (n=13/216), however only 1 was related to PE. When comparing with other treatments, Buckley (2022) found no statistically significant difference in 30-day readmission rate between the mechanical thrombectomy group (11%) and the routine care group (13%).

Device failure

One study, Sedhom 2021, specifically reviewed device failure reports for the Indigo aspiration system used for aspiration thrombectomy. It found that the most common failure mode was a Lightning Unit malfunction (36%, n=24) followed by rotating haemostasis valve malfunction (31%, n=21), resistance during use (15%, n=10) and aspiration failure (12%, n=8).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they have never happened (theoretical).

They listed the following anecdotal or theoretical adverse events not reported in the literature:

- DVT
- Infection
- Cardiac complications; tamponade, myocardial infarction, valvular dysfunction
- Iodine anaphylaxis
- Contrast nephropathy
- Haemothorax
- Puncture site pseudoaneurysm
- Stroke (clot transit through patent foramen ovale).

Three professional expert questionnaires were submitted for this procedure. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

The main evidence summary included 6 studies, including 4 prospective single-arm studies (3 trials and 1 registry), 1 retrospective comparative study and 1 database review. All 6 studies were in USA populations, included small sample sizes with the largest being 250 participants, and had short term follow-up. Variable inclusion criteria were used and many of the studies included intermediate-risk or sub-massive PEs either solely or in combination with high-risk or massive PEs. All of these factors may impact on the outcomes and on the generalisability to the UK population. The FLARE-ED sub-study by Jaber (2020) is less generalisable as it has a smaller sample of patients presenting via the Emergency Department only. The longest follow-up period was 6 months and so there is a lack of data on long-term outcomes in this group. The included studies generally reported fairly consistent outcomes, with statistically significant

improvements in markers of right ventricular function and low MAE and mortality rates in the short-term follow-up.

Various techniques and devices are used for mechanical thrombectomy. The main evidence summary includes 4 studies which use the FlowTriever device and 2 which use the Indigo aspiration system. There are other devices with varying techniques available for this procedure, some of which are covered in the additional studies in table 5. This variability means that the outcomes may not be generalisable to other techniques and devices, and caution should be taken in interpreting outcomes for this procedure.

Due to the non-randomised nature of the studies and lack of comparator, the study samples may be subject to selection bias as those included are not randomly selected. Buckley (2022) was the only study to include a comparator arm but was performed retrospectively and was not randomised. The comparator of routine care was heterogenous in terms of treatments used and the study did not include any measures of right ventricular function. There may be information bias in terms of the way the cases are managed and the outcomes recorded when participants are in a trial. Loss to follow-up may also introduce bias in the outcome reporting. Sedhom (2021) was a review of the MAUDE safety database which relies on voluntary reporting of events, it therefore will not capture all events so introduces selection bias. It also will not capture all mechanical thrombectomy events being performed so an incidence rate can't be calculated as there is no denominator available. The review was retrospective in nature and doesn't correlate device failure to clinical outcomes.

The FLARE study and FLARE-ED sub-study were sponsored by Inari medical, the manufacturers of the FlowTriever device, and they were involved in study design and data collection. Various authors of Toma (2022) are consultants for Inari medical and various other manufacturers including Penumbra. A couple of authors for Sedhom (2021) are consultants for various manufacturers including

Inari Medical. Sista (2021) was funded by Penumbra and the authors have consultant roles for various companies including Penumbra and Inari medical.

There are gaps in the evidence overall and for particular patient populations such as those with Patent Foramen Ovale (PFO). Further evidence is needed from randomised controlled trials with larger populations and longer-term follow-up. There are some ongoing trials which may help to address some of the evidence gaps:

- STRIKE-PE: A Prospective, Multicentre Study of the Indigo™ Aspiration System Seeking to Evaluate the Long-Term Safety and Outcomes of Treating Pulmonary Embolism NCT04798261. N=600, prospective cohort study. Study completion March 2026.
- FlowTriever for Acute Massive Pulmonary Embolism (FLAME). NCT04795167. N=250, prospective parallel-group cohort. Completion date May 2023.
- The PEERLESS Study. NCT05111613. N=550, Prospective, multicentre, RCT of the FlowTriever System compared to Catheter-Directed Thrombolysis (CDT) for acute intermediate-high-risk pulmonary embolism (PE). Completion date October 2023.
- Evaluating the Safety and Efficacy of the AlphaVac Multipurpose Mechanical Aspiration (MMA) F1885 PE for Treatment of Acute Pulmonary Embolism. NCT05318092. N=122, single arm trial. Completion date November 2023.
- FlowTriever All-Comer Registry for Patient Safety and Hemodynamics (FLASH). Observational (patient registry), n=1300. Completion date July 2023.

Related NICE guidance

Interventional procedures

- NICE's interventional procedures guidance 651 on Percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg (2019).
  Recommendation: special arrangements for acute iliofemoral DVT, research only for distal DVT.
- NICE's interventional procedures guidance 524 on Ultrasound-enhanced, catheter-directed thrombolysis for pulmonary embolism (2015).
  Recommendation: special arrangements.
- NICE's interventional procedures guidance 523 on Ultrasound-enhanced, catheter-directed thrombolysis for deep vein thrombosis (2015).
  Recommendation: special arrangements.

Technology appraisals

- NICE's technology appraisal guidance on:
    - Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism (2015) Technology appraisal guidance 341
    - Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism (2014) Technology appraisal guidance 327
    - Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism (2013) Technology appraisal guidance TA287
    - Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism (2012) Technology appraisal guidance TA261

Medical technologies

- None.

NICE guidelines

NICE guideline on Venous thromboembolic diseases: diagnosis, management and thrombophilia testing (2020) NICE guideline 158

Professional societies

- British Thoracic Society
- British Society of Interventional Radiologists
- The Vascular Society of Great Britain & Ireland
- British Society of Endovascular Therapy
- Society for Acute Medicine
- Royal College of Physicians of London
- Royal College of Physicians of Edinburgh
- Royal College of Physicians and Surgeons of Glasgow
- Society of Vascular Nurses
- Association of Surgeons of Great Britain and Ireland
- Society of Academic and Research Surgery

- Society for Vascular Technology of Great Britain and Ireland
- Vascular Anaesthesia Society of Great Britain & Ireland

Evidence from patients and patient organisations

NICE received 1 submissions from patient organisations about percutaneous thrombectomy for massive and submassive pulmonary embolus.

NICE received 0 questionnaires from patients who had the procedure (or their carers).

Patients' views on the procedure were consistent with the published evidence and the opinions of the professional experts [See the patient commentary summary for more information.]

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 3 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

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2. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. JACC Cardiovasc Interv. 2021 Feb 8;14(3):319-329. doi: 10.1016/j.jcin.2020.09.053. Epub 2021 Jan 13. PMID: 33454291.
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2019 May 13;12(9):859-869. doi: 10.1016/j.jcin.2018.12.022. PMID: 31072507.

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10. Vedovati MC, Germini F, Agnelli G, Becattini C. Prognostic role of embolic burden assessed at computed tomography angiography in patients with acute pulmonary embolism: systematic review and meta-analysis. J Thromb Haemost. 2013 Dec;11(12):2092-102. doi: 10.1111/jth.12429. PMID: 24134450.

Methods

NICE identified studies and reviews relevant to percutaneous thrombectomy for massive and submassive pulmonary embolus from the medical literature. The following databases were searched between the date they started to 18th August 2022: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with massive and submassive pulmonary embolism.
- Intervention or test: percutaneous mechanical thrombectomy
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	19/08/2022	1946 to August 18, 2022
MEDLINE In-Process (Ovid)	19/08/2022	1946 to August 18, 2022
MEDLINE Epubs ahead of print (Ovid)	19/08/2022	August 18, 2022
EMBASE (Ovid)	19/08/2022	1974 to 2022 August 18
EMBASE Conference (Ovid)	19/08/2022	1974 to 2022 August 18
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	19/08/2022	Issue 8 of 12, August 2022
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	19/08/2022	Issue 7 of 12, July 2022
International HTA database (INAHTA)	19/08/2022	-

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

1 Thrombectomy/ 9486
2 percutaneous.tw. 139833
3 1 and 2 1184
4 (percutaneous adj4 thrombectom*).tw. 564
5 3 or 4 1279

6 catheter*.tw. 198862
7 Catheters/ 6814
8 (mechanical* adj4 thrombectom*).tw. 3581
9 or/6-8 203262
10 5 and 9 636
11 Venous Thromboembolism/ 14419
12 ((Venous adj4 (thrombo-embolism* or thromboembolism*)) or VTE).ti,ab. 23485
13 Pulmonary Embolism/ 42217
14 (((Pulmonary or lung*) adj4 embol*) or PE).ti,ab. 83515
15 Venous Thrombosis/ 28631
16 (((vein* or ven*) adj4 thromb*) or DVT).ti,ab. 83500
17 (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or embol*).ti,ab. 331968
18 (blood adj4 clot*).ti,ab. 11774
19 or/11-18 397581
20 10 and 19 554
21 EKOS.tw. 72
22 21 and 19 63
23 (Indigo adj4 Aspiration).tw. 19
24 FlowTriever*.tw. 29
25 AlphaVac.tw. 0
26 or/20,22-25 652
27 Animals/ not Humans/ 5004253
28 26 not 27 638
29 limit 28 to english language 596

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5.

Table 5 additional studies identified

Case reports, case series ≤20 without unique safety/efficacy outcomes and non-systematic narrative reviews have not been included in table 5.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Akbarshakh Akhmerov, Heidi Reich, James Mirocha, Danny Ramzy; Effect of Percutaneous Suction Thromboembolectomy on Improved Right Ventricular Function. Tex Heart Inst J 1 April 2019; 46 (2): 115–119. doi: https://doi.org/10.14503/THIJ-17-6551	N=13, AngioVac, median follow-up 74 days	77% survival to hospital discharge. Pre-procedure 8 (62%) had severe right ventricular dysfunction, post procedure this was 2 (17%) (p=0.031). 3 patients had intraprocedural haemodynamic instability leading to conversion to open surgery and standard cardiopulmonary bypass. Three in-hospital deaths, unrelated to procedure.	Small sample, short follow-up
Al-Hakim R, Park J, Bansal A, Genshaft S, Moriarty JM. Early Experience with AngioVac Aspiration in the Pulmonary Arteries. J Vasc Interv Radiol. 2016 May;27(5):730-4. doi: 10.1016/j.jvir.2016.01.012. PMID: 27106647.	N=5: 4 massive PE AngioVac	2/5 (40%) technical success (reduction in Miller Index ≥5). 4/5 deaths (80%) at mean of 7.3 days post procedure, of which 1 related to right ventricular free wall perforation.	Small sample, retrospective
Bonvini RF, Roffi M, Bounameaux H, Noble S, Müller H, Keller PF, Jolliet P, Sarasin FP, Rutschmann OT, Bendjelid K, Righini M. AngioJet rheolytic thrombectomy in patients presenting with high-risk pulmonary embolism and cardiogenic shock: a feasibility pilot study. EuroIntervention. 2013 Apr 22;8(12):1419-27. doi: 10.4244/EIJV8I12A215. PMID: 23680957.	N=10 (high risk PE and cardiogenic shock). Angiojet Follow-up to 3 months	In 2, IV thrombolysis given due to progressive haemodynamic deterioration following procedure. 7/10 patients died in the first 12 hours post-procedure (4 refractory right heart failure). 3/10 patients favourable outcomes and normalisation of RV function, no PE recurrence at 1 year.	Small sample, short follow-up, single centre.

Bunc M, Steblovnik K, Zorman S, Popovic P. Percutaneous mechanical thrombectomy in patients with high-risk pulmonary embolism and contraindications for thrombolytic therapy. Radiol Oncol. 2020 Feb 14;54(1):62-67. doi: 10.2478/raon-2020-0006. PMID: 32061168; PMCID: PMC7087421.	N=25 (high-risk PE) Follow-up to hospital discharge. 56%: pigtail catheter 44%: Aspirex device	Non-significant improvements in systemic blood pressure and heart rate. Statistically significant reduction in peak systolic tricuspid pressure gradient (57 ± 14 mm Hg vs 31 ± 3 mm Hg; p = 0.018). Technical success in 80% Salvage thrombolytic therapy in 8/25 (32%). 68% survival to hospital discharge. No statistically significant difference in technical success, survival or any other parameters between subgroups receiving thrombolysis and PMT and those who only received PMT apart from transfusion requirement (50% vs 12%, p=0.04). Major complications: 1 significant puncture site bleeding Minor complications: 6/25 (24%)- 5 transient bradycardia during catheterisation and 1 groin haematoma.	Small sample, retrospective

Bunwaree, S., Roffi, M., Bonvini, J.M., et al. (2013). AngioJet® rheolytic thrombectomy: a new treatment option in cases of massive pulmonary embolism. Interventional Cardiology, 5, 71-87.	N=197 Group A (massive PE) = 76 Group B (massive + submassive PE) = 121 Systematic review of Angiojet rheolytic thrombectomy. Variable follow-up. 14 studies included: 9 (Group A) massive PE only 5 (Group B) massive and submassive PE combined population	Successful procedure (including clinical success/ technical success/ procedural successs) reported in 66/76 (86.8%) in group A, 99/105 (94.3%) group B. In Group A (reported in 5 studies) systolic PAP was reduced from pre-procedure: 55 ± 9.9 to post-procedure: 37.3 ± 18.8 and mPAP was reduced from pre-procedure: 37.8 ± 5.8 to post-procedure: 33.9 ± 8.2. In group B (reported in 4 studies) systolic PAP: pre-procedure, 48.7 ± 0.4 vs post-procedure, 37.9 ± 0.8; mPAP: pre-procedure 34.3 ± 4.9 vs post-procedure, 27.3 ± 1.2. Significance not reported. There were 31/197 (15.7%) major periprocedural events including 23 (11.6%) episodes of bradyarrhythmia and 2 (1%) transient asystole, out of which 18 (9.1%) required temporary pacemaker implantation. The review reported 6 (3%) intraprocedural deaths (all in group A)- 1 prior to device activation. The in-hospital mortality rate was 29/197 (14.7%): 13/76 (17.1%) in group A and 16/121 (13.2%) in group B. After discharge, no further deaths to 30 days. Major postprocedural events in 61/197 (30.1%) patients including 6 (3.0%) episodes of haemoptysis, 13 (6.6%)	Older systematic review referencing solely the Angiojet device. Country of origin not detailed for studies. All but 2 of the studies included fewer than 20 participants each and most were retrospective case series lacking comparator arms. Many of the studies did not report the clinical outcomes studied and in more than 40% of the patients included, thrombolysis was given which makes interpretation of the efficacy and safety of thrombectomy difficult. Three of the included studies (Bonvini, 2013; Margheri, 2008; Chechi, 2009) are also discussed separately.

		major inguinal haematomas, 2 (1%) episodes of melaena, 5 (2.5%) macro-haematuria, 2 (1%) retroperitoneal bleeding, 4 (2%) cerebral haemorrhage, 23 (11.7%) impaired renal function, 3 (1.5%) multiorgan failure and 7 (3.5%) significant thrombocytopaenia.	
Chechi T, Vecchio S, Spaziani G, Giuliani G, Giannotti F, Arcangeli C, Rubboli A, Margheri M. Rheolytic thrombectomy in patients with massive and submassive acute pulmonary embolism. Catheter Cardiovasc Interv. 2009 Mar 1;73(4):506-13. doi: 10.1002/ccd.21858. PMID: 19235240.	N=51 Angiojet Massive and submassive PE Average follow-up 35.5 ± 21.7 months	Technical success in 92.2% Statistically significant improvement in obstruction, perfusion and Miller index in all subgroups of severity ($p<0.0001$) and in systolic PAP ($p<0.05$). 4/51 major bleeding events (7.8%) 8/51 (15.7%) in-hospital mortality (6 due to persistent/refractory shock) 3 further deaths at long term follow-up unrelated to procedure/PE	Small sample, retrospective.

Cherfan P, Abou Ali AN, Zaghloul MS, Yuo TH, Phillips DP, Chaer RA, Avgerinos ED. Propofol administration during catheter-directed interventions for intermediate-risk pulmonary embolism is associated with major adverse events. J Vasc Surg Venous Lymphat Disord. 2021 May;9(3):621-626. doi: 10.1016/j.jvsv.2020.08.026. Epub 2020 Aug 26. PMID: 32858244.	N=340 Of which: 85 catheter directed thrombolysis, 229 ultrasound-assisted thrombolysis, 26 suction thrombectomy.	36 patients (10.6%) received propofol; 304 patients (89.4%) received midazolam plus fentanyl, morphine, or hydromorphone. Overall, 18 patients had ≥1 MAE (10 intubations, 11 decompensations, 2 surgical conversions, 3 deaths). Propofol group had a statistically significantly greater adverse event rate (13.8%) vs no-propofol group (4.2%; p=0.015). 16 patients experienced major bleeding or other procedure-related events (stroke in 4 (1.17%), coronary sinus perforation in 1, tricuspid valve rupture in 1, and the need for transfusion in 10 patients). Type of intervention was not a predictive factor for any outcome.	Majority of patients had catheter thrombolysis, only 26 suction thrombectomy. Reviewing effect of anaesthetic rather than intervention directly. Retropsective.

Ciampi-Dopazo JJ, Romeu-Prieto JM, Sánchez-Casado M, Romerosa B, Canabal A, Rodríguez-Blanco ML, Lanciego C. Aspiration Thrombectomy for Treatment of Acute Massive and Submassive Pulmonary Embolism: Initial Single-Center Prospective Experience. J Vasc Interv Radiol. 2018 Jan;29(1):101-106. doi: 10.1016/j.jvir.2017.08.010. Epub 2017 Nov 6. PMID: 29102272.	N=18 Indigo Aspiration System Follow-up to discharge (median hospital stay 10 days)	Technical success in 17/18 (94.4%) and clinical success in 15/18 (83.3%). Statistically significant improvement in right ventricle size (46.36 mm ± 2.2 before treatment vs 41.79 mm ± 7.4 after; p=0.041). Two patients died with massive PE and one patient died with submassive PE. Mortality= 16.7%. Of the 4 patients who received thrombolysis, 2 experienced intracranial bleeding and 1 abdominal bleeding.	Small sample, short follow-up.
Donaldson, C.W., Baker, J.N., Narayan, R.L., Provias, T.S., Rassi, A.N., Giri, J.S., Sakhuja, R., Weinberg, I., Jaff, M.R. and Rosenfield, K. (2015), Thrombectomy using suction filtration and veno-venous bypass: Single center experience with a novel device. Cathet. Cardiovasc. Intervent., 86: E81-E87	N=14, AngioVac Mean follow-up 23 days	Indications included intracardiac mass (73%), acute PE (33%), and caval thrombus (73%). Four patients (27%) were in shock at the start of the procedure. Successful evacuation of mass in 73%. Peri-procedure mortality was 0% and in-hospital mortality 13% at a mean follow-up of 23 days. No pulmonary haemorrhages, strokes or myocardial infarctions. 73% had a post procedural drop in haematocrit with 6 of these 11 requiring transfusion. Two patients required subsequent embolectomy (one open).	Small sample, short follow-up, focuses more on right heart thrombi.

Dukkipati, R., Yang, E., Adler, S. et al. Acute kidney injury caused by intravascular hemolysis after mechanical thrombectomy. Nat Rev Nephrol 5, 112–116 (2009). https://doi.org/10.1038/ncpneph1019	N=1 Case report Angiojet	43F, 8 weeks pregnant Bilateral PE treated with Angiojet system. Intraprocedural bradycardia. Post-procedural massive intravascular haemolysis and acute kidney injury. 48 hours in ICU, haemodialysis until day 21. Fetal loss on day 7. Renal function returned to normal on day 25.	Case report.
Dumantepe, M., Teymen, B., Akturk, U. and Seren, M. (2015), The Efficacy of Rotational Thrombectomy on the Mortality of Patients with Massive and Submassive Pulmonary Embolism. J Card Surg, 30: 324-332. https://doi.org/10.1111/jocs.12521	N=36 Massive and submassive PE Aspirex percutaneous aspiration device. Mean follow-up 14.3±5.8 months.	Complete thrombus clearance (≥90%) in 83.3% and near-complete (50% to 90%) clearance in 13.8%. Statistically significant decrease (56%) in mean PAP post-procedure. Major complication rate 6.3%. Two in-hospital deaths (one from refractory shock). Two patients had a significant bradycardic episode. No major bleeding events. Total 360-day survival was 88.8%.	Small sample, retrospective case series

Eid-Lidt G, Gaspar J, Sandoval J, de los Santos FD, Pulido T, González Pacheco H, Martínez-Sánchez C. Combined clot fragmentation and aspiration in patients with acute pulmonary embolism. Chest. 2008 Jul;134(1):54-60. doi: 10.1378/chest.07-2656. Epub 2008 Jan 15. PMID: 18198243.	N=18, follow-up 12.3 ± 9.4 months. Massive PE.	Statistically significant increase in systolic blood pressure post-procedure and statistically significant decrease in mean PAP (37.1 ± 8.5 mmHg vs 32.3 ± 10.5 mmHg, p = 0.0001). In-hospital major complication rate 11.1%, one death from refractory shock. One patient had intracerebral haemorrhage with minor neurologic sequelae (deemed to be secondary to local fibrinolytic therapy). Two transitory decreases in oxygen saturation during procedure (Aspirex device) without haemodynamic instability.	Small sample
Eid-Lidt G, Gaspar J, Sandoval J, et al. Persistent pulmonary hypertension and right ventricular function after percutaneous mechanical thrombectomy in severe acute pulmonary embolism. Eur Respir J 2017; 49: 1600910 [https://doi.org/10.1183/13993003.00910-2016]	N=52 Mean follow-up 40.2 ± 16.7 months. Excluded 8 for prior pulmonary artery hypertension, 8 for right ventricular hypertrophy and 5 for follow-up < 6 months. 7 patients died in hospital and were not included in analysis.	After the procedure, the shock index (1.1±0.23 vs 0.7±0.1; p=0.019), heart rate (113±14 vs post-86±13 bpm; p=0.005) and systolic systemic arterial pressure (100±14 vs 124±13 mmHg; p=0.005) improved. No recurrence of pulmonary embolism in-hospital. Four patients were re-admitted to hospital, two patients for recurrence of severe pulmonary embolism (4.1%) and two for complicated pneumonia. Overall survival (extra-hospital phase) at 5 years was 96.2%. Improvements in right ventricular function were mainly in the first 6 months with a 24% reduction in PAP.	Small sample

Escobar GA, Burks D, Abate MR, Faramawi MF, Ali AT, Lyons LC, Moursi MM, Smeds MR. Risk of Acute Kidney Injury after Percutaneous Pharmacomechanical Thrombectomy Using AngioJet in Venous and Arterial Thrombosis. Ann Vasc Surg. 2017 Jul;42:238-245. doi: 10.1016/j.avsg.2016.12.018. Epub 2017 Apr 13. PMID: 28412100.	N=102 (n=52 Angiojet, n=50 catheter-directed thrombolysis) Follow-up 3 days	Acute kidney injury (AKI) occurred in 29% of patients treated with Angiojet vs 8% of catheter-directed thrombolysis. Odds for AKI increased by Angiojet (OR 8.2, 95% CI 1.98-34.17, p=0.004). Concomitant open surgery and drop in haematocrit also raise the odds of AKI.	Includes use of Angiojet catheter with thrombolytic drugs, includes various arterial and venous thromboses so not specific to PE.
Gayen S, Upadhyay V, Kumaran M, Bashir R, Lakhter V, Panaro J, Criner G, Dadparvar S, Rali P. Changes in Lung Perfusion in Patients Treated with Percutaneous Mechanical Thrombectomy for Intermediate-Risk Pulmonary Embolism. Am J Med. 2022 Aug;135(8):1016-1020. doi: 10.1016/j.amjmed.2022.03.028. Epub 2022 Apr 22. PMID: 35469736.	N=3 Intermediate risk PE. FlowTriever Use of imaging for perfusion tracking	Pre-procedure and post-procedure perfusion estimation: Case 1: perfusion score improved from 5/15 pre-procedure to 12/15 within 48h and 13/15 at 3 months. Case 2: 7/15 pre-procedure to 8/15 within 72h, 10.5/15 at 3 months and 12/15 at 9 months. Case 3: 6/15 pre-procedure to 7/5/15 within 72h and 9/15 at 3 months. Overall, average lung perfusion score increased from 6/15 (40%) pre-procedure to 9.17/15 (61.1%) immediately post-procedure and 11.33/15 (75.6%) at last follow-up. No PE-related readmission within 30 days or PE-related complications.	Small sample

Graif A, Patel KD, Wimmer NJ, Kimbiris G, Grilli CJ, Upparapalli D, Kaneria AR, Leung DA. Large-Bore Aspiration Thrombectomy versus Catheter-Directed Thrombolysis for Acute Pulmonary Embolism: A Propensity Score-Matched Comparison. J Vasc Interv Radiol. 2020 Dec;31(12):2052-2059. doi: 10.1016/j.jvir.2020.08.028. Epub 2020 Nov 9. PMID: 33183975.	N=52 CDT group=26 Large-bore aspiration thrombectomy (LBAT)=26 (FlowTriever for majority)	Statistically significant decrease in systolic PAP, diastolic PAP, mean PAP, HR, and Miller score in both groups. Systolic PAP: Baseline and final systolic PAP was similar between the two groups (LBAT: 54.5 mm Hg ± 12.9 vs CDT: 54.5 mm Hg ± 16.3 at baseline, P=0.8; and LBAT: 42.5 mm Hg ± 14.1 vs CDT: 42.6 mm Hg ± 12.1, P =0.8, respectively). Heart rate: reductions not statistically significantly different between the 2 groups: (LBAT: -5.4 bpm ± 19.2 vs CDT: -9.6 bpm ± 15.8, P=0.4). Miller score: CDT demonstrated a higher reduction (-10.1 ± 3.9 vs -7.5 ± 3.8, P=0.02). Complications: LBAT had 1 minor haemorrhagic complication and 2 procedure-related deaths vs CDT resulted in 1 minor and 1 major haemorrhagic complication. ICU stay: 18/26 LBAT group and 26/26 CDT, p=0.004. Similar hospital length of stay.	Small sample, retrospective, propensity matched, non-randomised.

Kumar N, Janjigian Y, Schwartz DR. Paradoxical worsening of shock after the use of a percutaneous mechanical thrombectomy device in a postpartum patient with a massive pulmonary embolism. Chest. 2007 Aug;132(2):677-9. doi: 10.1378/chest.06-1082. PMID: 17699140.	Case report, unique safety information. Angiojet	31F, onset 1h post-caesarean section. Obstructive shock due to PE. Rheolytic thrombectomy removed obstruction and restoration of PA flow. Immediately post procedure refractory shock, cor pulmonale, gross haematuria and drop in haemoglobin secondary to fragmentary haemolysis. Haemolysis and shock resolved within 24h, remaining hospital course uneventful, and the patient discharged on day 7. An outpatient echocardiogram shortly after discharge revealed normal biventricular function and PAP.	Small sample, older report.

Margheri M, Vittori G, Vecchio S, Chechi T, Falchetti E, Spaziani G, Giuliani G, Rovelli S, Consoli L, Biondi Zoccai GG. Early and long-term clinical results of AngioJet rheolytic thrombectomy in patients with acute pulmonary embolism. Am J Cardiol. 2008 Jan 15;101(2):252-8. doi: 10.1016/j.amjcard.2007.07.087. PMID: 18178417.	N=25 (8 severe haemodynamic compromise, 12 moderate, 5 mild) Angiojet Median follow-up 61 months.	Technical and procedural success 100% Statistically significant improvement in obstruction, perfusion and Miller indexes overall, and in each subgroup (all p values <0.001). Statistically significant improvement in all above seen in patients given local fibrinolysis (n=8) and in those not given local fibrinolysis (n=17, p<0.05). 4/25 (16%) in-hospital mortality (2 persistent shock, 1 cerebral haemorrhage, 1 recurrence of embolism). All others alive at long-term follow-up except 1 noncardiopulmonary cause. Temporary transvenous pacing in 3 (12%) for bradycardia. 10 major haematomas requiring transfusion (40%). 7 postprocedural worsening of renal function (28%)	Small sample, retrospective, no comparator.
Martillotti, G, Boehlen, F, Robert-Ebadi, H, Jastrow, N, Righini, M, Blondon, M. Treatment options for severe pulmonary embolism during pregnancy and the postpartum period: a systematic review. J Thromb Haemost 2017; 15: 1942–50.	Systematic review N=7 for percutaneous thrombectomy	Maternal survival 100% Two cases went on to further treatments. Risk of fetal death 25% Risk of major bleeding 20% All reported good angiographic results without procedure-related complications. One case, a rheolytic thrombolysis complicated by severe haemolysis (paper included separately).	Different modalities used in different cases (systematic review including a number of case reports). Small sample size.

Morrow KL, Kim AH, Plato SA 2nd, Shevitz AJ, Goldstone J, Baele H, Kashyap VS. Increased risk of renal dysfunction with percutaneous mechanical thrombectomy compared with catheter-directed thrombolysis. J Vasc Surg. 2017 May;65(5):1460-1466. doi: 10.1016/j.jvs.2016.09.047. Epub 2016 Nov 19. PMID: 27876521.	N=145 Retrospective comparative review, single centre. 4 groups: Percutaneous mechanical thrombectomy (PMT) alone (n=15), PMT with tissue-plasminogen activator (tPA) pulse-spray, PMT (n=42) with catheter directed thrombolysis (CDT) (n=70), or CDT only (n=18). Follow-up to 6 months.	The overall incidence of renal dysfunction was 15%. The incidence was highest in the PMT/tPA pulse group (21%), followed by the PMT group (20%) and the PMT/CDT group (14%). CDT was not associated with renal dysfunction (0%). PMT (p=0.046), and PMT/tPA pulse (p=0.033) were associated with higher rates of renal dysfunction than the CDT controls. Renal dysfunction was higher in the arterial thrombus (21%) than venous thrombus (12%) groups. Stratified by the RIFLE (Risk, Injury, Failure, Loss, and End-stage renal disease) criteria, 13 (9%) patients progressed to the risk category, 6 (4%) progressed to the injury category, and 3 (2%) progressed to the failure category. None of the patients progressed to dialysis within the same admission period. The average length of time for creatinine values to return to baseline was 5.1 ± 5.2 days. No difference in 6-month outcomes between procedural groups.	Assesses catheter therapies in all vasculature locations with only 11 in pulmonary vasculature. Retrospective, small sample.

Mously H, Hajjari J, Chami T, Hammad T, Schilz R, Carman T, Elgudin Y, Abu-Omar Y, Pelletier MP, Shishehbor MH, Li J. Percutaneous mechanical thrombectomy and extracorporeal membranous oxygenation: A case series. Catheter Cardiovasc Interv. 2022 Aug;100(2):274-278. doi: 10.1002/ccd.30295. Epub 2022 Jun 10. PMID: 35686535.	N=9 Follow-up 90 days Large bore thrombectomy and ECMO	2/9 minimal thrombus retrieval (1 given salvage systemic thrombolysis, 1 converted to surgical embolectomy) Median ECMO duration 5 days (2.3-11.6) Median ICU stay 10 days (1.5-25.5) Median hospitalisation 16.1 days (1.5-30.9) 90 day mortality 22%	Small sample, combined treatment with ECMO. Results reporting limited.
Pelliccia F, De Luca A, Pasceri V, Tanzilli G, Speciale G, Gaudio C. Safety and Outcome of Rheolytic Thrombectomy for the Treatment of Acute Massive Pulmonary Embolism. J Invasive Cardiol. 2020 Nov;32(11):412-416. PMID: 33130592.	N=33 patients contraindicated to thrombolysis. Angiojet rheolytic thrombectomy. Follow-up 1 year	Angiographic improvement 32/33 (96%) Rapid improvement in functional class (3.3 ± 0.9 to 2.1 ± 0.7; P<0.001) Increase in oxygen saturation (71 ± 15% to 92 ± 17%; P<0.001) No deaths, no major bleeding, no renal failure. Post procedure anaemia in 4/33 (12.1%) Periprocedural side effects: Transient heart block (n=1, 3%) Hypotension (n=3, 9%) Bradycardia (n=5, 15.1%) At 1 year follow-up (n=30): PAP statistically significantly lower than baseline (65 ± 31 mm Hg vs 31 ± 19 mm Hg; P<0.001).	Small sample, no comparator.

Qureshi AM, Petit CJ, Crystal MA, Liou A, Khan A, Justino H. Efficacy and safety of catheter-based rheolytic and aspiration thrombectomy in children. Catheter Cardiovasc Interv. 2016 Jun;87(7):1273-80. doi: 10.1002/ccd.26399. Epub 2016 Feb 1. PMID: 26833887.	Included for consideration of paediatric population. Median age 1.9 months. Median follow-up 10 months. N=21 Rheolytic and aspiration thrombectomy.	Thrombectomy was performed in 50 vessels in 21 patients. Thrombectomy successful in 47/50 (94%) vessels in 18/21 (86%) patients. Additional balloon/stent therapy or tPA administration performed in 16/18 (89%) of these patients. 2 (9.5%) major complications (both with AngioJet): asystole when using activation times of >5 sec. At median follow-up 10 months: all 47 treated vessels patent and 8/18 (44%) required reintervention. Of the 4 pulmonary vessel patients, 2/4 (50%) thrombectomy successful, 3/4 Angiojet and1/4 pronto catheter.	Only 4/21 patients had PE. The rest had thrombosis in other vessels. Small sample, retrospective.

Nakazawa K, Tajima H, Murata S, Kumita S-I, Yamamoto T, And Tanaka K. Catheter fragmentation of acute massive pulmonary thromboembolism: distal embolisation and pulmonary arterial pressure elevation The British Journal of Radiology 2008 81:971, 848-854	Case series Rotating pigtail catheter N=25	Decrease in mPAP after thrombus fragmentation (34.2mmHg to 30.8mmHg, $p<0.05$) and after thrombolysis and thrombus aspiration (24.0 mmHg, $p<0.01$). Distal embolization occurred in 7/25 cases, in this group mPAP statistically significantly increased after thrombus fragmentation (34.1 to 37.9 mmHg, $p<0.05$) before statistically significantly decreasing after thrombolysis and aspiration (25.7mmHg, $p<0.05$). Statistically significant decrease in Miller Score after fragmentation (21.2 to 18.5, $p<0.01$) and aspiration (to 14.1, $p<0.01$). No recurrences observed. Continuous monitoring of mPAP can predict distal embolization and may improve safety.	Small sample All cases received local thrombolytic therapy as well.

Nezami N, Chockalingam A, Cornman-Homonoff J, Marino A, Pollak J, Mojibian H. Mechanical thrombectomy for pulmonary embolism in patients with patent foramen Ovale. CVIR Endovasc. 2020 Nov 28;3(1):89. doi: 10.1186/s42155-020-00180-9. PMID: 33247349; PMCID: PMC7695793.	Case series N=9 (3 high-risk and 6 intermediate/high risk) FlowTriever	Included for unique patient group (PFO). Technical success rate 100% Clinical success rate 77.8% Right heart-strain improved in 6/8 mPAP statistically significantly decreased (36.0 ± 15.2 vs 23.4 ± 8.4 mmHg, p<0.012) 1 patient developed middle cerebral artery embolic stoke 1 day post-procedure (unclear if related to procedure). No in-hospital mortality	Small sample, retrospective

Toma, C, Khandhar, S, Zalewski, AM, D'Auria, SJ, Tu, TM, Jaber, WA. Percutaneous thrombectomy in patients with massive and very high-risk submassive acute pulmonary embolism. Catheter Cardiovasc Interv. 2020; 96: 1465– 1470. https://doi.org/10.1002/ccd.29246	Mulit-centre case series N=34 Massive and very high-risk submassive PE. FlowTriever Mean follow-up 205 days.	Clot removal successful in 32/34 (94.1%). Procedural failure 2/34, both deteriorated during procedure and one died (2.9%). Decompensation following intubation (known profound negative haemodynamic effect in large PEs). Cardiac index improved from 2.0 ± 0.1 L/min/m2 before thrombectomy to 2.4 ± 0.1 L/min/m2 after (p = 0.01). The mPAP decreased from 33.2 ± 1.6 mmHg to 25.0 ± 1.5 mmHg (p = 0.01). Procedure. In 6 patients, cardiac index decreased post-procedure but additional vasopressors not required. At 24 hr blood pressures and heart rates statistically significantly improved. No complications directly attributable to device. No major treatment-related bleeding events. Statistically significant drop in haemoglobin was noted at 24 hr (12.2 ± 0.5 g/dL to 10.5 ± 2.2 g/dL, p = 0.007). The average length of stay was 9.8 ± 1.6 days. 33/34 (97%) survival to 205 days.	Small sample, no comparator.

Wible BC, Buckley JR, Cho KH, Bunte MC, Saucier NA, Borsa JJ. Safety and Efficacy of Acute Pulmonary Embolism Treated via Large-Bore Aspiration Mechanical Thrombectomy Using the Inari FlowTriever Device. J Vasc Interv Radiol. 2019 Sep;30(9):1370-1375. doi: 10.1016/j.jvir.2019.05.024. Epub 2019 Jul 30. PMID: 31375449.	N=46 (8 massive, 38 submassive). Retrospective case series. FlowTriever Follow-up 30 days post discharge.	Technical success 100% mPAP improved statistically significantly for all (33.9 ± 8.9 mm Hg before, 27.0 ± 9.0 mm Hg after; P < 0.0001) Intraprocedural reduction in mPAP in 88%. Survival to discharge 100% 2 MAEs (4.6%): haemoptysis requiring intubation, procedure-related blood loss requiring transfusion. No procedure-related deaths within 30d of discharge.	Small sample, single-centre, no comparator.